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Substitute for form 1449A/PTO			Complete if Known		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Application Number	10/114,909	
			Filing Date	April 3, 2002	
			First Named Inventor	Stanley M Crain	
			Art Unit	1614	
			Examiner Name	Raymond J. Henley III	
Sheet	1	of	1	Attorney Docket Number	96700/748

U.S. PATENT DOCUMENTS					
Examiner Initials [*]	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
	1	US- 5,580,876	12-03-1996	Crain et al.	
	2	US- 5,585,348	12-17-1996	Crain et al.	
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FOREIGN PATENT DOCUMENTS						
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		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)				
	3	EP 0 352 361 A1	01-31-1990	The Rockefeller University		

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Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Application Number	09/261,361
				Filing Date	March 3, 1999
				First Named Inventor	Stanley M. Crain
				Group Art Unit	1614
				Examiner Name	Ray Henley
Sheet	1	of	3	Attorney Docket Number	96700/453

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	1	CHAMI, et al., Treatment of Constipation-Predominant Irritable Bowel Syndrome (IBS-C) with the Opioid Antagonist Nalmefene Glucuronide (NG), The American Journal of Gastroenterology 1993, 88(9), 1568.	
	2	FARTHING, New Drugs in the Management of the Irritable Bowel Syndrome, Drugs 1998:56(1), 11-21.	
	3	DAPOIGNY, et al., Efficacy of Peripheral Kappa Agonist Fedotozine versus Placebo in Treatment of Irritable Bowel Syndrome, Digestive Diseases and Sciences 1995, 40(10) 2244-2248.	
	4	DROSSMAN, et al., Irritable Bowel Syndrome: A Technical Review for Practice Guideline Development, Gastroenterology 1997, 112:2120-2137.	
	5	DALTON, et al., Diagnosis and Treatment of Irritable Bowel Syndrome, American Family Physician 1997, 55(3):875-880.	
	6	CAMILLERI, et al., Review Article: Irritable Bowel Syndrome, Aliment. Pharmacol. Ther. 1997, 11:3-15.	
	7	PACE, et al., Therapy of Irritable Bowel Syndrome - An Overview, Digestion 1995, 56:433-442.	
	8	DELVAUX, et al., Trimebutine: Mechanism of Action, Effects on Gastrointestinal Function and Clinical Results, The Journal of International Medical Research 1997, 25:225-246.	
	9	DAPOIGNY, et al., Neurophysiology and Neuropsychiatry of the IBS, Digestion 1997, 58:1-9.	
	10	JUNIEN, et al., Review Article: The Hypersensitive Gut - Peripheral Kappa Agonists as a New Pharmacological Approach, Aliment. Pharmacol. Ther. 1995, 9:117-126.	
	11	GUE, et al., The K Agonist Fedotozine Modulates Colonic Distention - Induced Inhibition of Gastric Motility and Emptying in Dogs, Gastroenterology 1994, 107:1327-1334.	

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Sheet	2	of	3		

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	12	DROSSMAN, et al., Psychosocial Factors in the Irritable Bowel Syndrome, Gastroenterology 1988, 95:701-8.	
	13	DROSSMAN, et al., U.S. Householder Survey of Functional Gastrointestinal Disorders, Digestive Diseases and Sciences, 1993, 38(9):1569-1580.	
	14	TALLEY, et al., Medical Costs in Community Subjects with Irritable Bowel Syndrome, Gastroenterology 1995, 109:1736-1741.	
	15	KONIECZKO, et al., Antagonism of Morphine-Induced Respiratory Depression with Nalmefene, Br. J. Anaesth. 1988, 61:318-323.	
	16	WANG, et al., Morphine Tolerance and Physical Dependence: Reversal of Opioid Inhibition to Enhancement of Cyclic AMP Formation, Journal of Neurochemistry 1995, 64(3):1102-1106.	
	17	JOSHI, et al., Effects of prophylactic Nalmefene on the Incidence of Morphine-related Side Effects in Patients Receiving Intravenous Patient-controlled Analgesia, Anesthesiology 1999, 90:1007-11.	
	18	XU, et al., Opioids Can Enhance and Inhibit the Electrically Evoked Release of Methionine-Enkephalin, Brain Research 1989, 504:36-42.	
	19	GINTZLER, Relevance of Opioid Bimodality to Tolerance/Dependence Formation, Advances in Experimental Medicine and Biology, 373:73-83.	
	20	HORAN, et al., Antinociceptive Profile of Biphalin, a Dimeric enkephalin Analog, The J.I of Phar. and Exper. Ther. 265(3):1446-1454.	
	21	CHESKIN, et al., Assessment of Nalmefene Glucuronide as a Selective Gut Opioid Antagonist, Drug and Alcohol Dependence 1995, 39:151-154.	
	22	GAN, et al., Opioid-sparing Effects of a Low-dose Infusion of Naloxone in Patient-administered Morphine Sulfate, Anesthesiology 1997, 87:1075-81.	

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	23	CRAIN, et al., Modulation of Opioid Analgesia, Tolerance and Dependence by Gs -coupled, GM1 Ganglioside-regulated Opioid receptor Functions, TIPS 1998, 19:358-365.	
	24	CRAIN, et al., GM1 Ganglioside-induced Modulation of Opioid Receptor-mediated Functions, Annals of the New York Academy of Sciences 1998:106-125.	
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	26	SHEN, et al., Nerve Growth Factor Rapidly Prolongs the Action Potential of Mature Sensory Ganglion Neurons in Culture, and This Effect Requires Activation of Gs-coupled Excitatory k-Opioid Receptors on These Cells, The Journal of Neuroscience 1994, 14(9):5570-5579.	
	27	SHEN, et al., Ultra-low Doses of Naltrexone or Etorphine Increase Morphine's Antinociceptive Potency and attenuate Tolerance/Dependence in Mice, Brain Research 1997, 757:176-190.	
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	29	SHEN, et al., Chronic Selective Activation of Excitatory Opioid Receptor Functions in Sensory Neurons Results In Opioid 'Dependence' Without Tolerance, Neuroscience 1992, 597:74-83.	
	30	CRAIN, After Chronic Opioid Exposure Sensory Neurons Become Supersensitive to the Excitatory Effects of Opioid Agonists and Antagonists as Occurs After Acute Elevation of GM1 Ganglioside, Brain Research 1992, 575:13-24.	
	31	CRAIN, et al., Opioids can Evoke Direct Receptor-Mediated Excitatory Effects on Sensory Neurons, Pharmacological Sciences 1990, 11(2):77-81.	
	32	CRAIN, et al., Ultra-low Concentrations of Naloxone Selectively Antagonize Excitatory Effects of Morphine on Sensory Neurons, Thereby Increasing its Antinociceptive Potency and Attenuating Tolerance/Dependence During Chronic Cotreatment, Proc. Natl. Acad. Sci. (USA) 1995, 99:10540-10544.	
	33	SHEN, et al., Dual Opioid Modulation of the Action Potential Duration of Mouse Dorsal Root Ganglion Neurons in Culture, Brain Research 1989, 491:227-242.	

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